2 to dihydrogen and paraformaldehyde provides the previously prepared dihydride $(silox)_3TaH_2$ (**8**, >95%, ^1H NMR) and formaldehyde complex $(silox)_3Ta(\eta^2\text{-}CH_2O)$ (**9**, >95%, ^1H NMR),[10] respectively.

The potent reducing ability of $(silox)_3Ta$ (**2**) in combination with the stability of the $Ta(\mu\text{-}C_2)Ta$ bridge and Ta=O bond appears to mimic the surface properties responsible for the heterogeneous dissociation of CO. Further reactivity studies of **2**, mechanistic investigations pertaining to the formation of the dicarbide **4**, and detailed analyses of the latter will be reported in due course.

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(21) Anal. Calcd for **7**, $TaSi_3O_3C_{40}H_{87}$: C, 54.51; H, 9.95. Found: C, 54.50; H, 9.89. ^1H NMR (C_6D_6) δ 1.27 (s, silox, 81 H), 2.59 (s, $\equiv CCH_3$, 6 H); $^{13}C\{^1H\}$ NMR δ 30.68 (silox-CH_3), 23.37 (SiC), 22.05 ($\equiv CCH_3$), $H_3CC\equiv$ not observed.

Radical Cyclization-Trapping in the Synthesis of Natural Products. A Simple, Stereocontrolled Route to Prostaglandin $F_{2\alpha}$

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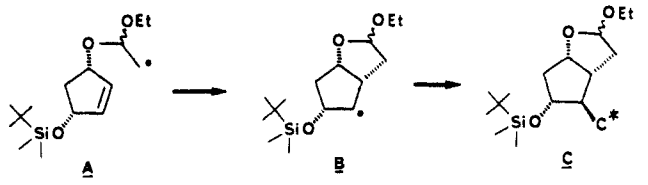
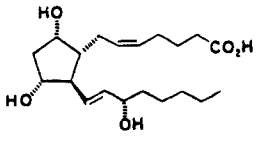
We report here an efficient synthesis of natural (+)-prostaglandin $F_{2\alpha}$ (**1**)[1] in which our recently described radical cyclization-trapping methodology[2] is utilized to add, in a single step, two differentiated carbon-functional appendages (precursors of the two side chains) to a preexisting cyclopentenediol nucleus. The two new carbon-carbon bonds are formed with virtually complete regio- and stereochemical control: The cyclization step (A → B) adds a potential acetaldehyde unit to the proximal end of the double bond and cis to the controlling allylic oxygen. Attachment of C* (B → C), the precursor of the unsaturated alcohol chain,





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† W.H.O. visiting fellow from the Shanghai Institute of Planned Parenthood Research (1982-1983).

(1) For recent surveys of prostaglandin syntheses, see: Pike, J. E.; Morton, D. R. *Chemistry of Prostaglandins and Leukotrienes*; Raven Press: New York, 1985. Lai, S. M. F.; Manley, P. W. *Nat. Prod. Rep.* **1984**, *1*, 409. Roberts, S. M.; Scheinmann, F. *New Synthetic Routes to Prostaglandins and Thromboxanes*; Academic Press: New York, 1982.

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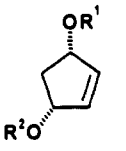
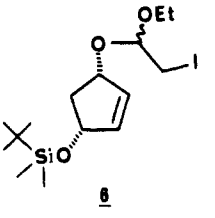
then takes place on the convex face of the bicyclic radical intermediate **B**. In this particular case, it is likely that the steric bulk of the silyloxy substituent magnifies the normal bias for convex face trapping.

Our synthesis began with cyclopentadiene, which is easily converted to *cis*-2-cyclopentene-1,4-diol (**2**) by photooxygenation-reduction.[3] The corresponding diacetate **3** (acetic anhydride, pyridine, methylene chloride, room temperature; 86%) is a convenient source of the (-)-monoacetate **4**.[4] Protecting group manipulation [(1) *tert*-butyldimethylsilyl chloride, imidazole, methylene chloride, room temperature; (2) potassium cyanide, ethanol, room temperature[5]] gave the monosilyl ether **5** in quantitative yield. The mixed iodoacetal **6**, necessary for radical cyclization-trapping, was obtained in 96% yield from **5** (ethyl vinyl ether, *N*-iodosuccinimide, methylene chloride, -20 °C).[2]



$R^1 = R^2 = H$ **2**
$R^1 = R^2 = Ac$ **3**
$R^1 = Ac, R^2 = H$ **4**
$R^1 = H, R^2 = Si(t\text{-}Bu)Me_2$ **5**

We now describe two sequences from **6** to **9** based on two different catalytic cyclization-trapping reactions. In the first



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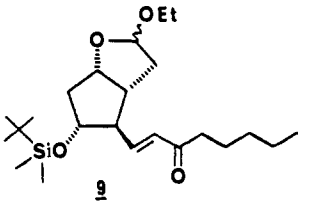
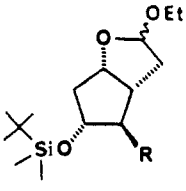


9



R = CN **7**
R = CHO **8**
$R = CH_2CH(TMS)C(=O)C_5H_{11}$ **10**
$R = CH_2CH{=}C(OTMS)C_5H_{11}$ **11**

of these, use of *tert*-butyl isocyanide as the radical trap[2,6] led to **7**, an obvious precursor of enone **9**. In the second sequence, simultaneous transfer of all eight carbons of the enone chain was achieved. We were intrigued by this approach because it required finding a solution to an important problem. Although vinyl ketones are suitable as traps in catalytic cyclization-trapping reactions,[2] use of 1-octen-3-one as the trap would yield a nearly symmetrical saturated ketone. Regiospecific introduction of a conjugated double bond into this ketone would not be simple. We show below that the use of an α-silyl-substituted vinyl ketone, 2-(trimethylsilyl)-1-octen-3-one, provided a solution to the problem.[7]

In the first route, which was carried out on a gram scale, the cyano compound **7** was obtained in 71% yield[8] from **6** (0.1 equiv

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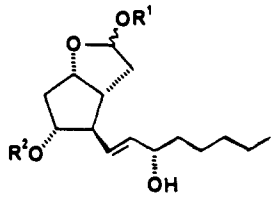
of tributyltin chloride, 2 equiv of sodium cyanoborohydride, 20 equiv of *tert*-butyl isocyanide, 0.1 equiv of AIBN, *tert*-butyl alcohol, reflux, 5 h).[9] Having the acid chain precursor masked as a cyclic acetal made the conversion of **7** to **9** an uneventful exercise via reduction to the aldehyde **8** (DIBAl-H, toluene, −20 °C; 84%), followed by keto phosphonate condensation (lithium chloride, $(i\text{-Pr})_2$NEt, diethyl 2-oxoheptylphosphonate, acetonitrile, room temperature;[10] 93%).

In the second route, radical cyclization–trapping (0.1 equiv of tributyltin chloride, 2 equiv of sodium cyanoborohydride, 7 equiv of 2-(trimethylsilyl)-1-octen-3-one, *hν* (254 nm), THF, room temperature, 10 h[11]) gave the crude trimethylsilyl ketone **10**. Volatile impurities were removed under high vacuum at 80 °C, and thermal rearrangement (140 °C, neat[12]) produced the trimethylsilyl enol ether **11**, which was oxidized (palladium acetate, acetonitrile, room temperature[13]) directly to **9**. The overall yield for these three steps was 58%.

To complete the synthesis, **9** was reduced diastereoselectively [(*S*)-BINAl-H, THF, −100 °C;[14] 89%) to the allylic alcohol **12**.



$R^1 = Et$, $R^2 = SiMe_3$ **12**

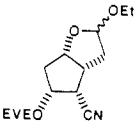
$R^1 = R^2 = H$ **13**

Hydrolysis (1.5% aqueous hydrochloric acid/THF (3:2), room temperature; 98%) gave the known dihydroxy lactol **13**.[15] Wittig reaction (potassium *tert*-butoxide, (4-carboxybutyl)triphenylphosphonium bromide, THF, room temperature;[15] 62%) produced $PGF_{2\alpha}$ (**1**) which was identical by TLC, ^{1}H NMR, ^{13}C NMR, and IR with an authentic sample.[16] The synthetic material had an optical rotation ($[\alpha]_{365}$ +78°; *c* 1.24 in 95% ethanol) essentially the same as that of the authentic $PGF_{2\alpha}$ ($[\alpha]_{365}$ +81°; *c* 1.55).

Acknowledgment. We thank the National Institutes of Health and the National Science Foundation for their financial support.

Supplementary Material Available: IR and NMR spectra of compounds in this paper (29 pages). Ordering information is given on any current masthead page.

(8) We have shown that without the α-silyloxy group the trapping ratio is 34:1 (ref 2, footnote 12). In the case of **7** we were unable to detect any of the undesired α-cyano isomer. Presumably, the steric bulk of the silyloxy group leads to production of even less of the unwanted epimer. Notably, the stereochemistry of the cyano group is not crucial to the success of the prostaglandin synthesis since the required β-isomer is the more stable of the two. This assumption was key to a number of routes which were followed before the cyclization–trapping process had been developed. In one such route, explored in the (±) series, radical cyclization (Bu_3SnH, AIBN, benzene, 80 °C) was performed with a cyano group already present on the cyclopentene system. Delivery of a hydrogen atom to the convex face of the bicyclic radical intermediate set the cyano stereochemistry of the product i as α. Epimeri-



i

zation of i to the β-cyano compound was then accomplished under base catalysis (K_2CO_3, methanol, room temperature, 2 days; 73%).

(9) Much of the excess of *tert*-butyl isocyanide can be recovered by codistillation with *tert*-butyl alcohol at the end of the reaction. The distillate contains *tert*-butyl cyanide (approximately one-third as much as isocyanide) which is formed by *tert*-butyl radical-mediated isomerization of the isocyanide. Nevertheless, it can be reused after adjusting the quantity of isocyanide to compensate for the isomerization. See: Meier, M.; Rüchardt, C. *Tetrahedron Lett.* **1983**, *24*, 4671.

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(14) Noyori, R.; Tomino, I.; Tanimoto, Y.; Nishizawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6709. Noyori, R.; Tomino, I.; Yamada, M.; Nishizawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6717. About 5% of the 15*R* epimer of **12** was also formed by using (*S*)-binaphthol of 91% ee. Independent reduction of the anomers of **9** allowed easy chromatographic separation of **12** from its undesired epimer.

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Reactivity of Group 4 Acyl Complexes with Alkylaluminum Reagents: Synthesis of Zirconium Ketone Complexes

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Transition-metal ketone complexes[1] and the closely related aldehyde[5,6] and ketene[7-9] complexes are of considerable interest because of their proposed role in CO reduction processes.[10] In this paper, we report a general and efficient synthesis of group 4 ketone complexes via the reductive alkylation of acyl complexes by alkylaluminum reagents. Mechanistic studies of this reaction reveal that aluminum reagents promote the intramolecular 1,2-migration of an alkyl group to a *cis*-acyl ligand to give ketone

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